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## REGULATION OF INNOVATION UNDER FOLLOW-ON BIOLOGICS LEGISLATION: FDA EXCLUSIVITY AS AN EFFICIENT INCENTIVE MECHANISM

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As part of its broader effort to reform the American health care system, Congress has recently enacted legislation that creates a statutory pathway for FDA approval of generic “follow-on” biologics products. A crucial debate leading up to the passage of this legislation was whether and to what extent it should provide originator biologics manufacturers with a period of FDA data exclusivity protection as an incentive for future innovation. This debate was particularly significant because of the ongoing reevaluation in the United States of the appropriate role of patent law in fostering technological advance, with recent Supreme Court decisions indicating a trend towards retrenchment of the scope of available patent protections. In the end, the bill adopted by Congress and signed into law by President Obama affords manufacturers of new biologics products with 12 years of data exclusivity.

The central thesis of this Article is that optimal biologics innovation policy would situate FDA exclusivity as the industry’s primary incentive mechanism, displacing patent law in that role. The inclusion of a lengthy 12-year data exclusivity period in the newly enacted legislation is a laudable step in the right direction. But reliance on patenting in the biologics innovation process would also likely have to be substantially curtailed in order to attain optimal levels of innovation. If this were achieved, FDA exclusivity would act as an adequate surrogate for the incentives offered by patents, while a number of pathologies currently associated with patenting in the biomedical research context would be eliminated.

This Article also argues that Congress should adopt a regime of *market* exclusivity protection instead of the *data* exclusivity protection

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presently included in the new legislation. Market exclusivity would permit the FDA to adopt rules requiring public disclosure of both basic research results (which may cease to be published absent strong patent rights) and clinical trials data (which cannot be divulged under a data exclusivity regime) in exchange for FDA approval. Such disclosure rules would contribute to efficient, disaggregated research into new and improved therapeutic approaches.

## I. INTRODUCTION

More than 30 years after Stanley Cohen and Herbert Boyer made the initial discoveries that ultimately led to modern techniques in biotechnology,<sup>2</sup> the biologics industry is flourishing. Biotechnology research has given and continues to give rise to a plethora of new human therapeutics, including gene-based therapies and recombinant protein products such as hormones, cellular growth factors, enzymes, clotting and anti-clotting factors, and monoclonal antibodies.<sup>3</sup> The importance of this industry to the future of medical science is buttressed by the fact that, in 2010, 50% of all new drugs approved by the U.S. Food and Drug Administration (“FDA”) are expected to be biologics,<sup>4</sup> and sales of biologics are expected to exceed \$60 billion.<sup>5</sup> However, the costs of these products are daunting and continue to escalate, imposing substantial deadweight losses on patients priced out of the market, and placing large burdens on private insurers and government health programs.<sup>6</sup>

Unlike the market for traditional small molecule pharmaceuticals, which has been increasingly subject to robust generic price competition in the wake of the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Act”), the biologics industry has been largely impervious to generic entry and price competition, and has been expected to remain so even as patents on key products expire.<sup>7</sup> The increasingly high cost of biologics has led many to contend that the industry’s imperviousness to generic competition should be remedied.

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<sup>2</sup> Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 Nw. U.L. Rev. 77, 93 (1999).

<sup>3</sup> David M. Dudzinski, *Reflections on Historical, Scientific, and Legal Issues Relevant to Designing Approval Pathways for Generic Versions of Recombinant Protein-Based Therapeutics and Monoclonal Antibodies*, 60 Food & Drug L.J. 143, 179 (2005).

<sup>4</sup> See Press Release, U.S. House of Representatives Comm. on Energy & Commerce, Bipartisan Group of Members Introduces “Promoting Innovation and Access to Life-Saving Medicines Act” (March 11, 2009), *available at* [http://energycommerce.house.gov/index.php?option=com\\_content&task=view&id=1528&Itemid=1](http://energycommerce.house.gov/index.php?option=com_content&task=view&id=1528&Itemid=1) [hereinafter Committee on Energy and Commerce Press Release].

<sup>5</sup> See Henry Grabowski, Ian Cockburn, & Genia Long, *The Market for Follow-On Biologics: How Will It Evolve?*, 25 Health Aff. 1291, 1291 (2006).

<sup>6</sup> Biologics now cost on average 22 times more per daily dose than small molecule pharmaceuticals, with the most expensive costing well over \$100,000 per year. See Committee on Energy and Commerce Press Release, *supra* note 4; see also Dudzinski, *supra* note 3, at 144 (noting protein-based therapeutics cost far in excess of \$10,000 per year on average).

<sup>7</sup> Henry G. Grabowski et al., *Entry and Competition in Generic Biologics*, 28 Managerial Decision Econ. 439, 439 (2007); see also Grabowski, Cockburn & Long, *supra* note 5, at 1298-99.

One of the main impediments to generic entry after patent expiration has been the absence of a clear statutory pathway to FDA approval of “follow-on” generic biologics.<sup>8</sup> In March 2009, in response to this regulatory lacuna, Representatives Waxman, Pallone, Deal, and Emerson introduced the Promoting Innovation and Access to Life-Saving Medicine Act, (“H.R. 1427”),<sup>9</sup> a bill designed to empower the FDA to approve generic versions of biologics. This effort followed several other attempts at follow-on biologics reform in prior legislative sessions.<sup>10</sup>

In the wake of Representative Waxman’s bill, Congress took up the follow-on biologics issue as part of its broader efforts to reform the American healthcare system. As a result, the Patient Protection and Affordable Care Act (“H.R. 3590”),<sup>11</sup> which recently passed both the House of Representatives and the Senate, and which President

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<sup>8</sup> In the traditional pharmaceuticals context, once patents on an originator product expire, the Hatch-Waxman Act authorizes the FDA to grant marketing approval to generic manufacturers that submit an Abbreviated New Drug Application (“ANDA”) and can demonstrate that their follow-on products are “bioequivalent” to the originator product. This pathway obviates the need for would-be generic competitors to conduct costly and redundant full-scale clinical trials in order to gain regulatory approval, thereby removing a core barrier to market entry. Instead, the FDA is empowered to approve an ANDA on the basis of clinical data submitted by the originator firm in its initial New Drug Application (“NDA”). The FDA has made it clear, however, that no equivalent statutory pathway currently exists for follow-on biologics. At present, any generic firms wishing to introduce competing follow-on biologics are required to submit an entirely new Biologics Licensing Application (“BLA”) (the equivalent of an NDA for small molecule drugs), which requires the completion of clinical trials for safety and efficacy. The FDA’s refusal to permit follow-on biologics manufacturers to utilize the abbreviated Hatch-Waxman pathway stems from the inherent difficulty of meeting the statutory requirement of “bioequivalence” in the context of large bio-molecules. See Dudzinski, *supra* note 3, at 193-99 (discussing regulatory approval regime); Grabowski, Cockburn, & Long, *supra* note 5, at 1292 (also discussing regulatory approval regime); see also U.S. Food and Drug Admin., *Omnitrope (somatropin [rDNA origin]) Questions and Answers*, May 30, 2006, <http://www.legalview.info/fda-alerts/449800/>. However, consensus is emerging that an effective abbreviated approval pathway can be achieved by employing a more lenient approval standard. See, e.g., Donna M. Gitter, *Innovators and Imitators: An Analysis of Proposed Legislation Implementing an Abbreviated Approval Pathway for Follow-on Biologics in the United States*, 35 Fla. St. U. L. Rev. 555, 590-609 (2008).

<sup>9</sup> Promoting Innovation and Access to Life-Saving Medicine Act, H.R. 1427, 111th Cong. (2009).

<sup>10</sup> See, e.g., Pathway for Biosimilars Act, H.R. 5629, 110th Cong. (2008); Patient Protection and Innovative Biologic Medicines Act of 2007, H.R. 1956, 110th Cong. (2007); Access to Life-Saving Medicines Act, H.R. 1038 & S. 623, 110th Cong. (2007).

<sup>11</sup> Patient Protection and Affordable Care Act, H.R. 3590, 111th Cong. (2009).

Obama signed into law on March 23, 2010,<sup>12</sup> contains provisions that enable the FDA to approve follow-on biologics products.<sup>13</sup>

Absolutely crucial to reform of the biologics industry is the issue of how to ensure continued robust innovation of new biologics products. Like the Hatch-Waxman regime for generic pharmaceuticals, the recently passed H.R. 3590 employs FDA data exclusivity protection as a regime of incentives. However, whereas H.R. 1427 initially proposed the same five-year data exclusivity period for originator biologics products that is currently available to innovator pharmaceutical firms under the Hatch-Waxman Act,<sup>14</sup> Congress ultimately decided to allocate a much longer period of 12 years in H.R. 3590.<sup>15</sup>

There is an ongoing debate as to whether such FDA exclusivity is a necessary mechanism to prevent erosion of incentives, or instead will be an unwarranted boon to the biologics industry in light of patent protections already available to innovator firms.<sup>16</sup> The central aim of this Article is to address the relative merits of FDA exclusivity compared to patent law as the appropriate primary incentive mechanism for continued innovation of biologics products. Examining this issue from a law and economics perspective, the main thesis of this Article is that an FDA-administered exclusivity period of properly calibrated length is a more efficient incentive regime than either (1) the system in place as of the date of H.R. 3590's passage, in which static deadweight losses

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<sup>12</sup> See Sheryl Gay Stolberg & Robert Pear, *Obama Signs Health Care Overhaul Bill, With a Flourish*, N.Y. Times, March 23, 2010, available at <http://www.nytimes.com/2010/03/24/health/policy/24health.html>.

<sup>13</sup> See Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 7001-03, 124 Stat. 119 (2010) (enacting Biologics Price Competition and Innovation Act of 2009, H.R. 3590, 111th Cong. (2009)). H.R. 3590 provides for the licensing of “biosimilar” and “interchangeable” biological products. See *id.* § 7002(a)(2). A follow-on product will be considered “biosimilar” if it is “highly similar” to the original product and “there are no clinically meaningful differences between the biological product and the [original] product in terms of the safety, purity, and potency of the product.” *Id.* § 7002(b)(3). A product will be considered “interchangeable” if it is biosimilar, it “can be expected to produce the same clinical result ... in any given patient,” and the risk of switching the patient one or more times between the original product and the biological product can be expected to be not significantly greater, in terms of safety or diminished effectiveness, than the risk of continuing to use the original product without such switching. *Id.* § 7002(a)(2). Approved interchangeable products “may be substituted for the [original] product without the intervention of the health care provider who prescribed the [original] product.” *Id.* § 7002(b)(3).

<sup>14</sup> See Press Release, U.S. House of Representatives Comm. on Energy & Commerce, Detailed Outline of the Promoting Innovations and Access to Life-Saving Medicine Act (March 11, 2009), available at [http://energycommerce.house.gov/index.php?option=com\\_content&task=view&id=1528&Itemid=1](http://energycommerce.house.gov/index.php?option=com_content&task=view&id=1528&Itemid=1).

<sup>15</sup> Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§ 7002(a)(2), 124 Stat. 119 (2010).

<sup>16</sup> See Grabowski, Cockburn & Long, *supra* note 5, at 1293-94.

resulting from the biologics industry's imperviousness to generic entry likely strongly outweigh any marginal incentives to innovate, or (2) a system with a mechanism for follow-on biologics approval, but that relies on patent law as its primary innovation policy tool. One implication of this thesis is that the inclusion of a lengthy FDA exclusivity period for new products in H.R. 3590 is a crucial first step in ensuring continued robust innovation in the biologics industry. To achieve optimal levels of innovation, however, a corresponding effort to reduce or eliminate reliance on patenting in the biologics innovation process will likely also be needed.

The analysis in this Article is divided into two parts. In Part I, I explore the FDA's role in innovation policy, and argue that employing FDA exclusivity instead of patent law as the primary driver of biologics innovation would remedy a number of identified pathologies currently associated with patenting. In Part II, I anticipate and respond to potential objections to reliance on FDA exclusivity as the primary incentive tool. Finally, I offer a brief summary of my conclusions.

## II. FDA EXCLUSIVITY IS SUPERIOR TO PATENT LAW

### A. FDA Regulation of Innovation

Though the FDA is ostensibly charged with protecting patients by ensuring the safety and efficacy of drugs, its function as a gatekeeper for entry into therapeutic markets has increasingly been employed as a tool of innovation policy.<sup>17</sup> Like patent law, an FDA-administered exclusivity period can effectively confer a monopoly on a market entrant, and thereby act as an incentive mechanism for firms to invest in the generation and clinical development of new medicines, and also in commercializing them.

The FDA administers two forms of exclusivity as incentive mechanisms: data exclusivity and market exclusivity. The former, employed in the Hatch-Waxman regime and now in H.R. 3590, prevents follow-on generic firms from relying on originator clinical trial data to obtain FDA approval. The latter, used under the Orphan Drug Act to induce investment into research on diseases with small patient populations, grants an applicant the exclusive right to market a product for a given clinical condition.<sup>18</sup> Market exclusivity confers a broader right because it prevents even generic firms willing to replicate clinical trials from entering the market, whereas data exclusivity does not.<sup>19</sup> I weigh the relative merits of utilizing data exclusivity and market exclusivity to stimulate biologics innovation in Part II, concluding that market exclusivity would be a superior policy. In this part, I argue in favor of FDA-administered exclusivity of either sort, and

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<sup>17</sup> See Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 Mich. Telecomm. & Tech. L. Rev. 345, 348 (2007).

<sup>18</sup> See Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation*, 19 Health Aff. 119, 123 (2001); see also Eisenberg, *supra* note 17, at 359-64 (2007).

<sup>19</sup> See Eisenberg, *supra* note 17, at 360.

against patent law, as the most appropriate primary incentive structure to ensure continued innovation in the biologics industry.

Before developing these arguments, it should be noted that this Article is in part agnostic on the appropriate length of the exclusivity period it advocates, except to say that the period should be calibrated to incentivize an optimal amount of investment into research, development, and commercialization of new biologics products, without needlessly extending restrictions on access to cheaper generic follow-on biologics beyond the point where marginal incentives are outweighed by additional deadweight loss. Such a calibration is a difficult exercise and a full-scale resolution of that question is beyond the scope of this Article.

Notably, the five-year exclusivity period advocated by Representative Waxman and the other sponsors of H.R. 1427 differs substantially from the 12-year period ultimately included in H.R. 3590, which tracks more closely the data exclusivity proposals in bills introduced in previous legislative sessions.<sup>20</sup> It is also substantially lower than the minimum 14-year exclusivity period advocated by the biotechnology industry, whose industry organization has argued that any shorter period would lead to an erosion of incentives to innovate new biologics products.<sup>21</sup> Waxman and his H.R. 1427 co-sponsors, by contrast, have argued that the five-year Hatch-Waxman data exclusivity period has been associated with robust innovation in the pharmaceutical context, and that therefore there is no need for longer data exclusivity for biologics. To buttress their argument, they point to data suggesting no difference between traditional drugs and biologics in terms of development costs or development timelines.<sup>22</sup>

The sponsors of H.R. 1427 perhaps overlooked two related points when they advanced this argument. First, robust innovation under the Hatch-Waxman regime might be occurring in spite of the overly short five-year period, because of longer periods of exclusivity enjoyed under pharmaceutical patent rights. Indeed, available data has demonstrated that the average effective patent life of a new drug is 11.7 years.<sup>23</sup> Second, a trend towards weakening patent rights and an emerging patent thicket problem in biomedical research, which will each be discussed further below, might lead one to

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<sup>20</sup> See, e.g., Patient Protection and Innovative Biologic Medicines Act of 2007, H.R. 1956, 110th Cong. (2007) (granting up to 15 years of exclusivity); Pathway for Biosimilars Act, H.R. 5629, 110th Cong. (2008) (proposing a 12-year period).

<sup>21</sup> See Biotechnology Indus. Org., *A Follow-On Biologics Regime Without Strong Data Exclusivity Will Stifle the Development of New Medicines* (Sept. 26, 2009) at 3-4, available at [www.bio.org/healthcare/followonbkg/FOBSMarket\\_exclusivity\\_20070926.pdf](http://www.bio.org/healthcare/followonbkg/FOBSMarket_exclusivity_20070926.pdf) [hereinafter BIO Follow-On Paper].

<sup>22</sup> See Press Release, U.S. House of Representatives Comm. on Energy & Commerce, Q's and A's on the "Promoting Innovation and Access to Life-Saving Medicine Act" (March 11, 2009) at 2, available at [http://energycommerce.house.gov/Press\\_111/20090311/Generic%20Biologics%20Q%20and%20A.pdf](http://energycommerce.house.gov/Press_111/20090311/Generic%20Biologics%20Q%20and%20A.pdf) (last visited Jan. 22, 2010) [hereinafter H.R. 1427 Q's and A's].

<sup>23</sup> See Henry G. Grabowski & John M. Vernon, *Effective Patent Life in Pharmaceuticals*, 19 Int'l J. Tech. Mgmt. 98, 116 (2000).

conclude that the patent regime is no longer adequate to confer sufficient market exclusivity for continued robust innovation in the life sciences industry.

The analysis I have stated above seems to suggest that a regulatory regime seeking to rely on FDA exclusivity as its primary incentive mechanism should adopt a period of roughly 12 years in order to replicate the average effective patent life of new pharmaceuticals. This is the exclusivity period ultimately included in H.R. 3590. Although the biotechnology industry believes this to be too short, one factor may mitigate their concern. It is expected that originator biologics products will inevitably continue to enjoy at least quasi-monopolistic pricing even beyond FDA exclusivity or patent term expiration. For example, the sponsors of H.R. 1427 anticipated that the FDA will have to require some level of clinical trials for at least the next several years, until advances in the understanding of bio-molecular structure make reliance on clinical studies unnecessary.<sup>24</sup> These supplementary clinical trials, and additional barriers unique to the biologics context (including substantially higher fixed production costs than traditional pharmaceuticals),<sup>25</sup> will make abbreviated approval significantly more costly than it is under the Hatch-Waxman Act. As a result, modeling by Grabowski demonstrates that, even in the absence of FDA exclusivity or patent barriers, generic entry will be somewhat limited under current technological conditions, leading to sustained high pricing.<sup>26</sup> As technological barriers are eliminated over time, however, the fixed costs of clinical trials and manufacturing will begin to recede,<sup>27</sup> and the appropriate length of FDA exclusivity may need to be revisited.

Having briefly addressed the proper length of exclusivity protection, I will use the remainder of this Part to set forth the arguments in favor of employing FDA exclusivity as the primary incentive mechanism for innovation in the biologics industry. Part II then addresses the potential costs of such a regime.

### *B. Arguments in Favor of FDA Exclusivity*

An FDA-administered exclusivity period should be the preferred primary incentive structure to promote biologics innovation because it would remedy the following four pathologies associated with the patenting of biomedical research: (1) the anti-commons problem in “upstream” research, (2) the reduction in *ex ante* incentives due to costs associated with obtaining and litigating patents and uncertainty over whether patents will be invalidated, (3) the incongruence between patent law standards designed to reward new inventions and the need to incentivize clinical trials of new medicines regardless of their patentability, and (4) the incompatibility of the fixed patent term with

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<sup>24</sup> See H.R. 1427 Q’s and A’s, *supra* note 22.

<sup>25</sup> See BIO Follow-On Paper, *supra* note 21, at 5-6.

<sup>26</sup> See Grabowski, Cockburn & Long, *supra* note 5, at 1296-98; *see generally*, Grabowski et al., *supra* note 7.

<sup>27</sup> Grabowski, Cockburn & Long, *supra* note 5, at 1297.



the inevitable lag time between the early filing of patents in the drug discovery process and final FDA marketing approval.

### 1. The Anti-Commons in Biomedical Research

The controversy over deploying FDA exclusivity in the newly adopted follow-on biologics legislation takes place in the context of an evolving U.S. patent system. In response to widespread concerns over a proliferation of unsound patents and to the perception that patent hold-up problems are unnecessarily stifling incentives in industries where innovation is primarily cumulative, the U.S. Supreme Court seems to be engaged in a program of tightening various patent law doctrines.<sup>28</sup> This program of reform has led to the concern that the already stringent standards for patentability in the context of biotechnology<sup>29</sup> will become even harder to satisfy, thereby decreasing incentives for innovation.<sup>30</sup>

Despite this apparent initiative to dial back legal protection in the unitary patent system, the pharmaceutical and biotechnology industries are generally seen as areas where patents, and the collection of monopoly rents made possible by them, are central to maintaining incentives for innovation of new products.<sup>31</sup> This perception has led to pressure from the life sciences industries for patent reform in the other direction.<sup>32</sup> Political economy considerations may render such unitary patent reform unlikely, however, given that the value of patents is being increasingly questioned in other sectors of the economy.<sup>33</sup>

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<sup>28</sup> See, e.g., *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 398 (2007) (tightening nonobviousness standard); *eBay Inc. v. Mercexchange L.L.C.*, 547 U.S. 388, 392 (2006) (holding that injunctive relief is not automatically available against patent infringers and expressing concern with patent hold-up problems).

<sup>29</sup> See, e.g., *Genentech v. Novo Nordisk*, 108 F.3d 1361, 1361 (Fed. Cir. 1997) (finding the patent on a method for generating human growth hormone invalid for lack of enablement); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1200 (Fed. Cir. 1991) (invalidating claims to a recombinant DNA version of erythropoietin for lack of enablement); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1559 (Fed. Cir. 1997) (invalidating claims to cDNA sequences encoding insulin for failure to meet written description requirement); *In re Fisher*, 421 F.3d 1365, 1365 (Fed. Cir. 2005) (finding that purified cDNA Expressed Sequence Tags (ESTs) fail to meet utility requirement of patentability); see also Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 *Nature Reviews Drug Discovery* 479, 480 (2008) (noting constrained scope of recent biological patents).

<sup>30</sup> See BIO Follow-On Paper, *supra* note 21, at 3.

<sup>31</sup> See Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 *Law & Contemp. Probs.* 289, 289 (2003); see also Eisenberg, *supra* note 18, at 120.

<sup>32</sup> Dan Burk & Mark Lemley, *Policy Levers in Patent Law*, 89 *Va. L. Rev.* 1575, 1634 (2003).

<sup>33</sup> Eisenberg, *supra* note 18, at 120.

In any event, strong patents in the biologics sector appear to be somewhat more of a mixed blessing than patent advocates assume. The traditional model of the pharmaceutical innovation process, whereby originator firms obtain a small number of broad patents on each new promising compound and then use those patents to recoup their R&D investments after regulatory approval, may not graft well onto the current biotechnology innovation space. The protection from competition conferred by patents once a product is on the market clearly remains an important source of innovation incentives. However, there is growing concern that, in the wake of the passage in 1980 of the University and Small Business Patent Procedures Act (the “Bayh-Dole Act”),<sup>34</sup> which encourages universities and other recipients of federal research dollars to patent their research,<sup>35</sup> the proliferation of intellectual property rights in “upstream” bioscience research—research that ultimately feeds into the development of final biologics products—is giving rise to “patent thickets” that are highly costly for product developers to navigate. Heller and Eisenberg dubbed this phenomenon the “tragedy of the anti-commons” in a frequently cited article in the journal *Science*.<sup>36</sup> The theory underlying this concern is that an anti-commons (a patent thicket) will emerge when multiple patent-holders each have a right to exclude others from using portions of an information pool. Because of transaction costs, strategic behavior, and cognitive biases of rights-holders, the theory asserts that rights will not be efficiently reallocated in such a way that the information pool is available for optimal use.<sup>37</sup>

In the case of biologics R&D, drug discovery has become dependent on basic knowledge of genes, proteins, biochemical pathways, and molecular techniques, as well as inputs such as reagents, genetically engineered animals, and databases.<sup>38</sup> In an earlier time, much of this upstream research would have been freely available in the public domain for originator firms to develop further into new therapeutic strategies.<sup>39</sup> However, due in part to the Bayh-Dole regime, these types of inputs are now increasingly the subject of patenting efforts by universities and commercial biotechnology firms (these firms purport to fill an important niche between fundamental research and applied drug discovery). As a result, the development of commercial biologics products often requires the licensing of multiple upstream patents.<sup>40</sup> Not only do these patents hinder downstream research by allowing owners to charge a premium for their use (causing

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<sup>34</sup> University and Small Business Patent Procedures Act, 35 U.S.C. §§ 200-212 (2006).

<sup>35</sup> For a discussion of the Bayh-Dole regime, see Eisenberg, *supra* note 18, at 125.

<sup>36</sup> Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 *Sci.* 698, 698 (1998).

<sup>37</sup> *Id.*

<sup>38</sup> Rai & Eisenberg, *supra* note 31, at 289.

<sup>39</sup> See Heller & Eisenberg, *supra* note 36.

<sup>40</sup> *Id.*

some would-be users to be priced out of the market),<sup>41</sup> they also impose search costs, licensing transaction costs, hold-up problems, and royalty-stacking problems on downstream product developers.

The anti-commons problem is of such concern to innovator manufacturing firms that they have begun investing resources to produce upstream information themselves and place it in the public domain before universities and biotechnology companies can patent it. A prime example is the effort to prevent biotechnology companies and universities from patenting single nucleotide polymorphisms ("SNPs"), which are useful in research for finding disease-specific genes and in developing diagnostic tools. To prevent the patenting of SNPs, pharmaceutical companies have joined with the Wellcome Trust (a U.K. non-profit organization) to sponsor a consortium of researchers to identify SNPs and make their findings freely available.<sup>42</sup>

Though in theory patent pools and other institutions for bundling patent rights could reduce transaction costs and help to overcome anti-commons problems, these private mechanisms have failed to materialize in the biotechnology sector.<sup>43</sup> In fact, Heller and Eisenberg suggest that the enormity of the transaction costs involved, the heterogeneity of upstream owners, and the cognitive biases of rights-holders may prove to be an intractable set of problems to any future efforts at rights bundling.<sup>44</sup>

In sum, the proliferation of upstream patenting seems to have led to a substantial diminution in the size of the public domain available as a starting point for applied R&D.<sup>45</sup> Worse, this proliferation appears to have replaced the public domain with a thicket of overlapping patent claims in the hands of multiple independent owners, impeding originator firms' access to basic knowledge and acting as a drag on incentives to develop, clinically test, and commercialize final biologics products.<sup>46</sup> The relative superiority of FDA-administered exclusivity compared to patents with respect to this anti-commons problem lies in the ability of FDA exclusivity to offer similar monopoly protection to originator biologics firms as an incentive to gain regulatory approval without the associated drag on incentives due to early-stage patenting. In a unitary patent

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<sup>41</sup> Rai & Eisenberg, *supra* note 31, at 295.

<sup>42</sup> *Id.* at 298.

<sup>43</sup> *Id.*

<sup>44</sup> See Heller & Eisenberg, *supra* note 36.

<sup>45</sup> It should be noted that some authors have questioned whether the current evidence establishing the existence of tragedy of the anti-commons problems in upstream biomedical research is large enough to warrant concern. See, e.g., Michael S. Mireles, *An Examination of Patents, Licensing, Research Tools, and the Tragedy of the Anticommons in Biotechnology Innovation*, 38 U. Mich. J.L. Reform 141, 174-94 (2004) (reviewing the evidence and finding it ambivalent).

<sup>46</sup> See Heller & Eisenberg, *supra* note 36; see also, generally, Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 Berkeley Tech. L.J. 813, 813 (2001), available at <http://eprints.law.duke.edu/1512/> (supporting the criticality of competition in the field of biopharmaceutical patents).

system, it would be difficult to fine tune patents such that the strength of final product patents was enhanced without also enhancing the strength of their upstream patent counterparts.<sup>47</sup> FDA exclusivity, by contrast, specifically tailors incentives to reward successful end-product development. This analysis suggests that gradual retrenchment of patent law in the biotechnology sector, combined with strong FDA exclusivity as an incentive to bring finished products to market, is the optimal regulatory structure.

## 2. Costs of Patent Enforcement

In addition to the potentially prohibitive transaction costs arising from biomedical anti-commons, biologics products developers face substantial costs associated with prosecuting and enforcing patents on products they seek to bring to market. One potentially alarming example of these types of costs is the frequency of patent challenges by generic pharmaceutical firms under the Hatch-Waxman regime.<sup>48</sup> The prospect of having to either pursue these lawsuits and risk patent invalidation or enter into costly reverse-payment settlements with generic challengers almost certainly reduces *ex ante* incentives to innovate. Additionally, the biotechnology industry organization has expressed concern that patent protection is narrower for biologics products than for pharmaceuticals and that, as a result, generic manufacturers will be able to easily design around biologics product patents to avoid infringement liability should biologics innovators attempt to litigate.<sup>49</sup> This concern may be overblown in light of the fact that, in order to rely on an originator's clinical data for abbreviated approval, a generic biologics company will still have to establish "biosimilarity" under H.R. 3590. It is unclear why one should expect this standard to be interpreted more broadly than the scope of biologics product patents.

In any event, utilizing FDA exclusivity as the primary incentive mechanism to drive innovation should entirely eliminate the above-discussed costs and uncertainty. Under FDA exclusivity, firms are relieved of the need to vigorously pursue patenting strategies and patent litigation in order to ensure their ability to recoup investment costs. They need not factor uncertainty over potential future invalidation of their patents and over potential future inability to secure infringement verdicts into their *ex ante* development and commercialization investment decisions. In fact, FDA exclusivity is guaranteed to any firms that successfully gain regulatory approval of new biologics. In contrast to the substantial costs associated with patenting, the only costs of obtaining FDA exclusivity are the expenditures necessary to comply with FDA marketing approval procedures, which firms must bear in any event to market their products.

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<sup>47</sup> See Eisenberg, *supra* note 18, at 124.

<sup>48</sup> See C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. Rev. 1553, 1553 (2006), available at [http://www2.law.columbia.edu/faculty\\_franke/Legal\\_Scholarship/Paying\\_For\\_Delay.pdf](http://www2.law.columbia.edu/faculty_franke/Legal_Scholarship/Paying_For_Delay.pdf); see also Grabowski, Cockburn & Long, *supra* note 5, at 1295-96.

<sup>49</sup> See BIO Follow-On Paper, *supra* note 21, at 1.

### 3. Unpatentable Biologics

Another important pathology associated with relying on the patent system as the primary incentive mechanism is that it leads to under-investment in clinical testing and commercialization of unpatentable drugs. This would not be a relevant concern if there were perfect congruence between the requirements of patentability (which incentivize the invention of new therapeutic candidates) and the need to incentivize the stages of product development between initial discovery and marketing approval. This is not the case, however. There are a host of reasons why a promising therapeutic candidate may fail patentability requirements, including prior disclosure through publication or the advent of recent scientific advances that make the candidate appear obvious in hindsight. Yet the relationship between the patentability of a therapeutic candidate and its potential social value if advanced through clinical testing is tenuous at best. Absent patent protection, any incentives to invest the enormous sums required to conduct clinical trials evaporate,<sup>50</sup> and, as a result, the social value that could be realized if these unpatentable products were brought to market is lost.<sup>51</sup> Indeed, this problem may be exacerbated in the current climate of receding patent strength, should a higher number of potential biologics products fail to meet the requirements of patentability.

One solution would be to relax the requirements of patentability in order to increase the number of candidate therapeutics with strong patent protection. This solution would be a blunt instrument, however. First, it could inflame the anti-commons and patent enforcement pathologies discussed above. Moreover, it would likely only partially remedy the problem given the structural discordance between patent law's goal of incentivizing the generation of new and non-obvious ideas, and the specific need in the biologics industry to promote downstream clinical testing and the commercialization of ideas. FDA exclusivity, by contrast, better tailors incentives for firms to bear these downstream development, regulatory approval, and commercialization costs for any socially valuable new drug, regardless of whether it meets the standards of patentability.<sup>52</sup>

### 4. Time Lag Between Patenting and Regulatory Approval

Finally, relying on patents to incentivize biologics research and development suffers from the problem that there is a significant lag time between the date a patent application on a potential new product is filed and the date of FDA regulatory approval.<sup>53</sup>

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<sup>50</sup> The average cost of clinical trials exceeds all other costs of developing a new biologics product combined. See Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 Managerial Decision Econ. 469, 469 (2007), available at <http://ideas.respec.org/a/wly/hlthec/v28y2007i4-5p469-479.html/>.

<sup>51</sup> See generally Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 Texas L. Rev. 503, 503 (2009), available at <http://www.texasrev.com/sites/default/files/issues/vol87/pdf/roin.pdf> (providing an in-depth discussion of this phenomenon in the pharmaceutical industry).

<sup>52</sup> See *id.* at 564-69.

<sup>53</sup> See Eisenberg, *supra* note 17, at 351.

Because the patent term is fixed at 20 years from the date of filing, the longer the development and approval horizon for a new drug, the shorter the period of post-approval market exclusivity an innovator firm enjoys. The effect of this inverse relationship is that there are robust incentives to invest in gaining approval of therapeutics for which clinical trial results are likely to be achieved quickly, whereas there are insufficient incentives to develop and market potentially socially valuable new therapeutics whose development timelines are too long.<sup>54</sup>

The Hatch-Waxman regime attempts to correct for this problem in the pharmaceuticals context by allocating patent term extensions of up to five years for delays in the regulatory approval process.<sup>55</sup> Yet this approach is only partially successful, given that regulatory delay is just one of several factors that feed into the lag time between patenting and market sales, and given that the lag time can eat up far more than five years of a patent term.

FDA exclusivity, by contrast, better alleviates this patent system pathology by allocating a uniform period of monopoly protection to firms who invest in the clinical development and commercialization of biologics products, regardless of how long it takes to move the product from the lab to the marketplace. Under this uniform monopoly period, one ought to witness a partial shift of resources away from projects with short clinical timelines towards some of the more daunting, yet more socially valuable, clinical projects whose length may be long relative to the patent term. In fact, an optimal approach would have the FDA tailor the length of the exclusivity period to the time and costs of clinical research and development. Such a regime may prove difficult to administer, however, and the specifics of how it might be achieved are beyond the scope of this Article.

### III. POTENTIAL OBJECTIONS

Part I developed a series of arguments in favor of employing FDA exclusivity as the primary incentive mechanism for biologics innovation. Reliance on FDA exclusivity instead of patent law may, however, give rise to a number of pathologies of its own, including: (1) erosion of incentives for upstream research absent strong patent protection, (2) dissipation, via rent-seeking behavior prior to obtaining FDA marketing approval, of the very same social gains associated with increased innovation under FDA

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<sup>54</sup> See Benjamin N. Roin, *The Perverse Incentives Created by the Patent Term for Drugs* (Feb. 19, 2009) (preliminary draft paper presented to Health Law & Policy Workshop at Harvard Law School); see also William M. Landes & Richard A. Posner, *The Economic Structure of Intellectual Property Law* 300 (2003) (discussing the related proposition that, despite correlation between the fixed costs of R&D and the degree of patent protection required to create adequate incentives, the patent system does not tailor patent protection to fixed costs of R&D).

<sup>55</sup> For a discussion of Hatch-Waxman patent term restoration, see Eisenberg, *supra* note 17, at 352.

exclusivity, and (3) impairment in the disclosure of socially valuable information encouraged by patents. This Part examines and addresses each of these in turn.

### *A. Upstream Incentives*

A first—and potentially powerful—critique of the regime this Article advocates is that a weakening of patent rights in the upstream stages of biotechnology innovation, and primary reliance on downstream FDA exclusivity instead, could lead to a collapse of incentives to invent research tools and other inputs into the creation of final biologics products. In the long term, such a collapse might ultimately lead to fewer candidate biologics products being generated for clinical testing, despite the availability of FDA exclusivity at the end of the process.

This concern is unwarranted, however, because other factors are likely to encourage robust upstream innovation in the absence of patent rights. The costs associated with recognizing property rights in upstream research (discussed in Part I, *supra*) should only be borne where the production and dissemination of information at this stage would be suboptimal in the absence of rights.<sup>56</sup> This Part argues that robust upstream biotechnology innovation will occur in the absence of patent rights for two reasons: (1) norms favoring scientific invention and open disclosure of the fruits of federally-funded basic biomedical research will ensure continued generation of upstream knowledge; and (2) strategic partnership arrangements between small biotechnology companies and originator manufacturing firms will convert upstream knowledge to downstream biologics candidates.

#### 1. The Norms of Science

Prior to the 1980s and the enactment of Bayh-Dole, basic molecular biology research was mostly governed by a system of norms adhered to by the academic scientific community. This normative system, though now in retreat, still exists. Its primary characteristics are that it: (1) discourages secrecy because of its inconsistency with the goals of feedback and independent verification, (2) denounces as immoral the assertion of rights in scientific discovery, (3) promotes the free dissemination of scientific information, and (4) lavishes the highest respect and recognition on those who make original contributions to scientific invention. Importantly, this last norm incentivizes scientists to vigorously compete to disclose their inventions.<sup>57</sup> Examples of these norms in action include: (1) Stanley Cohen and Herbert Boyer expressing skepticism about patenting gene-splicing techniques and demanding that those techniques be licensed non-exclusively and (2) Georges Kohler and Cesar Milstein, the developers of monoclonal antibody technology, determining that it was inappropriate to seek patents on their invention.<sup>58</sup> The thrust of these examples is that foundational biotechnology R&D was

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<sup>56</sup> See Landes & Posner, *supra* note 54, at 24.

<sup>57</sup> For a more in-depth treatment of this norm system, see Rai, *supra* note 2, at 88-94.

<sup>58</sup> *Id.* at 93-94.

not motivated by the promise of patents. Rather, other incentive structures, such as the desire for widespread respect and recognition, and the federal government's subsidization of basic research at universities and research institutes, were filling the gap.<sup>59</sup>

Things began to change significantly when, in 1980, the Supreme Court signaled a favorable attitude towards patenting genetic technologies.<sup>60</sup> Congress then passed the Bayh-Dole Act to encourage patenting of research conducted with federal sponsorship.<sup>61</sup> The rationale behind Bayh-Dole was not to incentivize basic science research, which was already robust. Rather, Bayh-Dole stemmed from a perception that the traditional normative system of open science was inefficient in terms of producing marketable products. The fear was that, because public disclosure preempted patenting, private firms would have little incentive to spend resources developing research ideas already in the public domain.<sup>62</sup>

Since the passage of the Bayh-Dole Act, intellectual property claims have permeated upstream research and the norms of scientific inquiry have been crowded out. Universities and federal grant recipients have sought patents on research inputs such as DNA sequences, protein structures, and disease pathways, converting to property what was once the domain of open science.<sup>63</sup> Specifically, in order to obtain patents, many of these actors have eschewed the norm of open disclosure, instead keeping scientific knowledge secret and refusing to share research material.<sup>64</sup>

Once patents are obtained, universities seek licensing agreements involving royalties or cash payments to transfer research tools to private industry.<sup>65</sup> Many argue that a large number of these upstream inventions were not difficult to identify and would have been developed regardless.<sup>66</sup> A relevant example is the discovery of the BRCA-1 and BRCA-2 breast cancer genes at the University of Utah and its exclusive license with Myriad Genetics.<sup>67</sup> The American Civil Liberties Union recently brought a lawsuit on behalf of a number of plaintiffs, including patients, universities, researchers, and medical

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<sup>59</sup> *Id.* at 119.

<sup>60</sup> *See Diamond v. Chakrabarty*, 447 U.S. 303, 303 (1980).

<sup>61</sup> University and Small Business Patent Procedures Act, 35 U.S.C. §§ 200-212 (2006).

<sup>62</sup> *See Rai*, *supra* note 2, at 95-96.

<sup>63</sup> *See Rai & Eisenberg*, *supra* note 31, at 289-91.

<sup>64</sup> *See Rai*, *supra* note 2, at 109-10.

<sup>65</sup> *See Rai & Eisenberg*, *supra* note 31, at 294.

<sup>66</sup> *See Rai*, *supra* note 2, at 119.

<sup>67</sup> *See CNN, ACLU Sues Over Patents on Breast Cancer Genes* (May 13, 2009), <http://www.cnn.com/2009/HEALTH/05/12/us.genes.lawsuit/index.html>.



associations, challenging the constitutionality of the patents on those genes.<sup>68</sup> They argue that Myriad and the University of Utah Research Foundation are using their patents to limit potentially valuable downstream research and to inhibit the free flow of information in violation of the First Amendment.<sup>69</sup> Additionally, the upstream patents on these genes have increased the cost of preventative genetic screening for women to upwards of \$3,000 per test.<sup>70</sup> It is unclear, however, whether the patents were necessary to motivate either the discovery of the BRCA genes or the subsequent research conducted upon them, potentially rendering the associated costs unjustified.<sup>71</sup>

At a more fundamental level, widespread patenting in the wake of Bayh-Dole may actually be causing federally funded researchers to shift their efforts away from basic science and towards more applied work, which could cause large social losses in the long term as fewer foundational discoveries are made.<sup>72</sup> Collective action problems likely stand in the way of individual institutions or researchers foregoing these patenting opportunities in favor of the public domain, however.<sup>73</sup>

The best solution to this set of problems is the removal of patent law from this space coupled with the reintroduction of scientific norms.<sup>74</sup> A unitary weakening of patent rights may partially achieve this, but a full-scale shift back in the direction of open science likely requires amendment or repeal of the Bayh-Dole Act. Under these conditions, federal funding and the norms of scientific inquiry could step in to assure

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<sup>68</sup> *Ass'n for Molecular Pathology v. United States PTO*, No. 09-4515, 2010 U.S. Dist. LEXIS 35418, at \*2 (S.D.N.Y. Apr. 5, 2010).

<sup>69</sup> *Id.* at \*17-18, \*162.

<sup>70</sup> *Id.* at \*58.

<sup>71</sup> On March 29, 2010, District Court Judge Robert Sweet issued a decision invalidating the patents on the BRCA-1 and BRCA-2 genes as improperly covering “laws of nature.” *Ass'n for Molecular Pathology v. United States PTO*, No. 09-4515, 2010 U.S. Dist. LEXIS 30629 (S.D.N.Y. Mar. 29, 2010), *amended by Ass'n for Molecular Pathology v. United States PTO*, No. 09-4515, 2010 U.S. Dist. LEXIS 35418 (S.D.N.Y. Apr. 5, 2010); *see also* John Schwartz & Andrew Pollack, *Judge Invalidates Human Gene Patent*, N.Y. Times, March 29, 2010, available at <http://www.nytimes.com/2010/03/30/business/30gene.html?src=me&ref=general>. If ultimately upheld on appeal, this ruling could have broad implications for biologics innovation, and could potentially help to alleviate some of the anti-commons problems associated with gene patenting.

<sup>72</sup> *See* Landes & Posner, *supra* note 54, at 316.

<sup>73</sup> *See* Rai & Eisenberg, *supra* note 31, at 305.

<sup>74</sup> Research inputs such as genes, ESTs, SNPs, reagents, and the like, should probably be distinguished from other inputs into the biologics innovation process, such as laboratory machinery (gene sequencing equipment, microscopes, etc). The latter may be better candidates for continued patenting because of the need to incentivize substantial private investment to develop them. *See id.* at 302. That said, other barriers to entry, such as lead time, fixed manufacturing costs, and brand loyalty, may sufficiently protect manufacturers of laboratory machinery so as to make patent law unnecessary.

continued, robust generation and dissemination of the kinds of basic science discoveries that serve as inputs into downstream biologics product development. Moreover, the policy rationale for Bayh-Dole (encouraging commercialization of government-sponsored inventions)<sup>75</sup> would not be impaired. While it is true that suboptimal levels of technology transfer occurred in the pre-Bayh-Dole era, this was likely a consequence of the doctrine of anticipation in patent law, which makes it impossible to obtain patents on publicly disclosed technological discoveries. Unable to rely on patents to recoup development and commercialization costs, firms would naturally shy away from investing in university-generated science that had already been published. Deploying FDA exclusivity as an incentive for downstream product development, however, helps eliminate this paradox by protecting biologic product developers from free-riding competition once products are brought to market, regardless of whether the technologies at the heart of those products are patented. Investment in the commercialization of publicly generated technology is thus incentivized without the costs associated with upstream patenting.

## 2. Strategic Partnerships

A potential objection to this solution is that it ignores the role of small biotechnology companies in converting publicly generated science into commercial applications. Small biotechnology companies are playing an increasingly important role in filling the innovation space between the research conducted at universities and the product development being done at large manufacturing firms.<sup>76</sup> Indeed, there are currently more than 1,500 biotechnology companies in the U.S., most of which are relatively small.<sup>77</sup> These companies rely extensively on patent portfolios to attract venture financing and equity capital. The important function carried out by these biotechnology firms could therefore be impaired without strong patent protection, to the detriment of downstream product innovation.

This objection at first appears strong, and, to be dealt with adequately, likely requires a more in-depth treatment than can be offered here. Nonetheless, this Article will attempt a preliminary answer to it. First, though patents seem central to start-up biotech firms' ability to secure venture funding,<sup>78</sup> a far larger source of capital for these firms comes from the partnership alliances they maintain with large pharmaceutical and biologics manufacturers.<sup>79</sup> In fact, start-up firms often experience difficulty attracting venture and equity financing until they secure their first strategic alliance with a large

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<sup>75</sup> *Id.* at 290.

<sup>76</sup> See Grabowski, Cockburn & Long, *supra* note 5, at 1294.

<sup>77</sup> See Dudzinski, *supra* note 3, at 178.

<sup>78</sup> See Grabowski, Cockburn & Long, *supra* note 5, at 1299.

<sup>79</sup> See Nadine Roijakkers & John Hagedoorn, *Inter-Firm R&D Partnering in Pharmaceutical Biotechnology Since 1975: Trends, Patterns, and Networks*, 35 Res. Pol'y 431, 433 (2006), available at <http://ideas.repec.org/a/eee/respol/v35y2006i3p431-446.html>.

originator firm. The structure of the biotech innovation space has evolved such that large manufacturers act as nodal players with multiple strategic partnerships with upstream biotechnology companies.<sup>80</sup> As evidence of the fruits of this structure, as of 2005, thirty percent of traditional pharmaceutical industry revenue was derived from biologics products obtained through partnership deals with smaller biotechnology companies.<sup>81</sup>

Despite the current reliance on patenting in this area, there is no reason to suppose that small biotech players could not protect the research conducted at this stage of the innovative process with trade secrecy law and contractual secrecy provisions instead. Under the incentive regime advocated by this Article, large manufacturers would continue to have incentives to partner with these companies (or to acquire them through M&A transactions) in order to enrich product pipelines, because any therapeutic candidates developed as trade secrets would later be protected by FDA exclusivity on the market.

Any concern that reliance on trade secrecy law causes innovators to shift resources away from research into products that can be easily reverse engineered (such as therapeutics) is unwarranted in this context. With FDA exclusivity employed as the primary incentive structure for finished biologics products, a candidate therapeutic approach need only be protected as a trade secret until the time of FDA regulatory approval, at which point disclosure would become irrelevant because the exclusivity period prevents reverse engineers from entering the market. Prior to FDA approval, potential reverse engineers could not access the product through market purchases, and so, with appropriate secrecy measures in place, ease of copying should be of no concern to developers.

Separately, there is evidence that inter-firm network formation and the free dissemination of knowledge through such networks is key to robust innovation at successful small biotech companies.<sup>82</sup> The role that patents may play in either advancing or retarding both network formation and knowledge dissemination seems ambiguous, and potentially deleterious. This further confounds the actual value of patents in this innovative space.

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<sup>80</sup> *Id.* at 431; *See also* William W. McCutchen Jr. & Paul M. Swamidass, *Motivations for Strategic Alliances in the Pharmaceutical/Biotech Industry: Some New Findings*, 15 J. High Tech. Mgmt. Res. 197, 197 (2004), *available at* [http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6W56-4CGMG5B-1&\\_user=18704&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_sort=d&\\_docanchor=&view=c&\\_searchStr1d=1116398852&\\_rerunOrigin=google&\\_acct=C000002018&\\_version=1&\\_urlVersion=0&\\_userid=18704&md5=c79578deec392a114002202c2ad3c8b1](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6W56-4CGMG5B-1&_user=18704&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_searchStr1d=1116398852&_rerunOrigin=google&_acct=C000002018&_version=1&_urlVersion=0&_userid=18704&md5=c79578deec392a114002202c2ad3c8b1).

<sup>81</sup> *See* Kerry A. Dolan, *Drug Alliance Alchemy*, *Forbes*, June 19, 2005, [http://www.forbes.com/2005/06/19/pharma-biotech-alliances-cz\\_kd\\_0619pharma.html](http://www.forbes.com/2005/06/19/pharma-biotech-alliances-cz_kd_0619pharma.html).

<sup>82</sup> *See, e.g.,* Jason Owen-Smith & Walter W. Powell, *Knowledge Networks as Channels and Conduits: The Effects of Spillovers in the Boston Biotechnology Community*, 15 Org. Sci. 5, 5 (2004), *available at* [http://www.stanford.edu/~woody/papers/knowledge\\_nets.pdf](http://www.stanford.edu/~woody/papers/knowledge_nets.pdf); Maija Renko, Malin Brannback & Alan Carsrud, *Sources, Development and Uses of Innovation in Modern Biotechnology*, 1 Int. J. Tech. Mgmt. 345, 345 (2008), *available at* [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=1344652](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1344652).

In sum, though the concern that patenting is important to the small biotechnology sector initially seems well-founded, it is actually less damaging to this Article's proposal when one considers that, with FDA exclusivity as the primary incentive mechanism for product development, other business models employing trade secrecy and contracting can fill the biotech niche in order to create vibrant product pipelines. Potential difficulties confronting a secrecy model of this sort are discussed further below. First, however, this Part analyzes the potential problem of rent dissipation.

### *B. Rent Dissipation*

A second potentially powerful critique of an incentive regime that combines FDA exclusivity with weak patent rights is that the absence of strong upstream patents might cause rent-dissipating competition to obtain FDA approval. This critique is rooted in the prospect theory of patent law, which posits that broad exclusive rights should be granted early in the inventive process because they permit efficient coordination of downstream research activities through licensing transactions by rights-holders.<sup>83</sup> Otherwise, the theory holds, competition between firms seeking to acquire those monopoly rents associated with being the first to commercialize an invention (in this case, because FDA exclusivity will confer product monopolies) will consume all or most of the potential social gains from that invention, converting expenses incurred by the losers of the race into deadweight social losses.<sup>84</sup>

This prospect theory of the economic function of patents, however, likely does not accurately portray their utility in the early and applied stages of biomedical research. Arti Rai has advanced a critique of this theory in biomedical research, which, when combined with my proposal to employ FDA exclusivity as the primary regime of incentives, weighs strongly against the need for strong upstream biotechnology patents. Her critique and its implications are explored below. Prospect theory may have more currency, though, when it comes to coordinating clinical trial testing of new candidate therapeutics because of the greater potential for rent-seeking behavior at this stage that would reduce social welfare. This too will be explored further below. Finally, potential rent dissipation issues after FDA approval are another concern that will be addressed below.

First, Arti Rai has advanced a compelling argument against the applicability of prospect theory with respect to upstream patenting in biomedical science. Her evidence suggests that "coordination by a single rights-holder undermines scientific creativity in both basic and applied research."<sup>85</sup> It appears that basic biomedical science occurs most quickly and most effectively when independent teams of scientists employ different

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<sup>83</sup> See, e.g., Edmund Kitch, *Nature and Function of the Patent System*, 20 J. L. & Econ. 265, 267-71 (1977).

<sup>84</sup> See Landes & Posner, *supra* note 54, at 17.

<sup>85</sup> See Rai, *supra* note 2, at 123.

approaches to the same or similar problems. Indeed, many scholars argue that innovation in this space is best understood as an evolutionary, or quasi-Darwinian, process of trial and error.<sup>86</sup> This view implies that many independent sources of inventive activity are superior to an early patentee directing a centralized process, in part because the prospector may have a flawed conception of the optimal path for future development, leading to a retardation of technological progress.<sup>87</sup> As discussed in Part I, *supra*, transaction costs and anti-commons problems may also inhibit the efficient allocation of upstream information to downstream developers, further stalling technical advance.<sup>88</sup> To place this argument into economic parlance, vigorous competition at these stages of research does not dissipate social gains, but instead either sufficiently speeds up innovation or produces a sufficient number of otherwise unavailable inventions, such that the increase in present value from competition offsets the added costs of uncoordinated research.

Rai suggests that this same logic holds for the more applied stages of biotechnology. In other words, taking an embryonic idea and converting it to potential therapeutic uses occurs most efficiently when many different teams or firms are independently investigating the issue.<sup>89</sup> Rai and Eisenberg discuss the example of the broad initial patent rights granted to the University of Wisconsin Research Foundation over pluripotent embryonic stem cell technology (a broad new territory of scientific inquiry). These rights were exclusively licensed to Geron Corporation, which, they argue, led to inefficiencies in developing that technology that could have been avoided by placing it in the public domain.<sup>90</sup>

Rai offers a useful framework for determining whether to grant upstream exclusive rights: any increased incentives (1) to devise basic research ideas in the first place and (2) to develop those initial ideas into useful products, should be compared to and balanced with (3) the costs of reduced creativity in developing uses for those ideas as a result of the loss of independent investigation and (4) the transaction costs of creating coordinated research through reallocation of rights.<sup>91</sup>

Applying Rai's framework to the biotechnology innovation process, granting exclusive rights in upstream research ideas is unlikely to be justifiable. For the reasons discussed above, these ideas are likely to be generated anyway because research at this stage is federally subsidized, because the costs of deriving these ideas are likely to be relatively low, and because the norms of scientific inquiry are likely to incentivize their creation in the absence of patents. The costs of converting initial discoveries into

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<sup>86</sup> See, e.g., Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839, 873-79 (1990); Landes & Posner, *supra* note 54, at 318.

<sup>87</sup> See Landes & Posner, *supra* note 54, at 319.

<sup>88</sup> See Rai & Eisenberg, *supra* note 31, at 297.

<sup>89</sup> See Rai, *supra* note 2, at 124-25.

<sup>90</sup> See Rai & Eisenberg, *supra* note 31, at 293, 309.

<sup>91</sup> See Rai, *supra* note 2, at 136-37.

therapeutic candidates, however, are likely to be high in biotechnology. Rai argues that these high costs do not justify granting exclusive rights to prospectors, though, because the creativity costs and transaction costs associated with doing so will outweigh any marginal increased incentives for development.<sup>92</sup>

Her argument carries even more weight with FDA exclusivity employed as the primary incentive mechanism for biologics innovation. If strategic partnership arrangements and trade secrecy (discussed *supra* Part II.A.2), combined with the promise of FDA exclusivity, can step in as incentives for biotechnology firms to develop and refine basic science ideas into clinical candidates, concerns that the absence of patents would deter product developers from investing in this stage of the innovative process should dissolve. Firms would bear these costs without patent protection because of the promise of FDA exclusivity, and, as such, the creativity and transaction costs caused by patenting upstream inventions would represent unjustified deadweight loss.

Rai's framework plays out differently when applied to the clinical trials phase, however, and suggests that an exclusive right is preferable once a candidate therapeutic is ready for clinical testing. First, the creativity costs associated with only one firm controlling the conduct of clinical trials are likely to be relatively low because a therapeutic strategy has already been developed and clinical design is relatively straightforward. Moreover, the additional transaction costs associated with an exclusive right at this stage should be relatively low because of the absence of troubling downstream anti-commons issues and because of the relatively few licenses required to facilitate a drug trial. In contrast, the cost of conducting clinical trials is enormous. The promise of FDA exclusivity should incentivize firms to bear those costs, but the social gains from bringing products through this phase could be entirely dissipated if multiple independent teams routinely conducted clinical trials on the same therapeutic candidate.

Rai's framework therefore suggests that it would be efficient to allocate prospecting rights to firms at the moment a product is ready for clinical testing. One relatively simple way to achieve this is to adopt a rule that the FDA cannot register the same product for more than one clinical trial.<sup>93</sup> This rule would prevent rent-dissipating competition while maintaining incentives to conduct clinical trials in order to gain FDA exclusivity upon marketing approval.

One final area in which a regime of FDA exclusivity combined with weak patent rights might cause socially deleterious rent dissipation is the period after a biologics product gains FDA marketing approval (i.e., once the product has completed clinical trials and is on the market). With data exclusivity employed as the primary incentive mechanism, competitors may have strong incentives to reverse engineer particularly profitable blockbuster biologics products, to independently conduct clinical trials on them, and then to seek FDA approval with an entirely independent licensing application (instead of utilizing the abbreviated pathway available under H.R. 3590), all to capture some of the monopoly rents accruing to the original innovator. In fact, this kind of activity had already been observed prior to H.R. 3590's passage. Despite the absence of a regime for follow-on biologics, six generic manufactures of human growth hormone

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<sup>92</sup> *Id.* at 125-29.

<sup>93</sup> See Roin, *supra* note 54, at 568.

("hGH") were able to obtain regulatory approval from the FDA by conducting their own comprehensive Phase III clinical studies to demonstrate safety and efficacy.<sup>94</sup>

The costs of redundant trials of this nature are likely to represent deadweight social loss if the trials all simply generate the same information about safety and efficacy. Moreover, the prospect of generic firms entering the market in this manner might reduce *ex ante* incentives for biologics innovators. The simplest way to remedy this form of rent dissipation would be to adopt FDA market exclusivity as the primary incentive mechanism, instead of the FDA data exclusivity protection contained in H.R. 3590. As discussed in Part I, a market exclusivity rule would prevent the FDA from granting regulatory approval to the same therapeutic compound during a specified period, regardless of whether a would-be competitor conducted independent clinical trials.

### C. Disclosure

A third potential critique of the incentive regime advocated by this Article is that the benefits of the disclosure function of patents might be lost because firms will elect to protect as much information as possible by trade secrecy.<sup>95</sup> While the production of conventional small molecule drugs has proven relatively straightforward, the manufacturing processes for larger bio-molecules are much more complicated.<sup>96</sup> This complexity could make biologics significantly more difficult to reverse engineer for would-be generic producers, who would otherwise have access to information disclosed in patents to assist them in developing follow-on products. This disclosure concern has merit, but can be dealt with in the following manner.

First, in the absence of upstream patents, the norms of scientific inquiry can be expected to encourage innovation and disclosure at the basic research phase.<sup>97</sup> Second, trade secrecy would indeed be expected to replace patent law as a mechanism to protect innovation by small biotechnology companies in the stages of innovation that take basic research and convert it to clinical trial-ready therapeutic candidates.<sup>98</sup> This concern should be mitigated, however, by the fact that the length of this applied research stage is likely to be relatively short, and in any event far less than the 20-year patent term. While patenting at this stage forces disclosure, the resultant patents permit their holders to exclude other would-be researchers from using the disclosed information, and there is no meaningful experimental use exception in the U.S. to mitigate that problem.<sup>99</sup>

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<sup>94</sup> See Grabowski, Cockburn, & Long, *supra* note 5, at 1293-94.

<sup>95</sup> For an in-depth discussion of the disclosure function of the patent system, see Landes & Posner, *supra* note 54, at 326-32.

<sup>96</sup> See Grabowski, Cockburn & Long, *supra* note 5, at 1293-94.

<sup>97</sup> See *supra* Part II.A.1.

<sup>98</sup> See *supra* Part II.A.2.

<sup>99</sup> See Rai, *supra* note 2, at 139.

Third, trade secrecy strategies after FDA marketing approval, which should be the most pressing concern, could be avoided by adopting the following three rules: 1) FDA *market* exclusivity instead of *data* exclusivity as the incentive mechanism, 2) a requirement that, in exchange for market exclusivity, firms disclose any manufacturing trade secrets necessary to make the product, and surrender any patents held on the product into the public domain, and 3) a requirement that the FDA publish all clinical trial data submitted for the purpose of gaining approval.

The second and third rules are designed to effectuate socially beneficial disclosure by innovator biologics firms. Under the second rule, disclosure of manufacturing trade secrets and product patents would (1) facilitate generic entry after expiration of the FDA exclusivity period, and (2) enable open, disaggregated research into new uses for, and improvements of, therapeutic products. Presently, the FDA treats clinical trial data submitted by originator firms as proprietary and not subject to disclosure.<sup>100</sup> By encouraging disclosure of this information, the third rule would lead to the following social gains: (1) doctors, patients, and insurers would have more information at their disposal to make informed drug choices, (2) firms could learn from each other's clinical trial experiences and use that information to design better clinical trials, (3) independent analyses and scrutiny of clinical trial results and regulatory decisions could be conducted, and (4) large-scale meta-analyses of data aggregated from multiple studies of related products could be carried out.<sup>101</sup> The first rule (FDA market exclusivity instead of data exclusivity) would be necessary to make feasible the second and third rules. Data exclusivity as the primary incentive mechanism is incompatible with these latter rules because a free-riding generic competitor (1) could use disclosed manufacturing secrets to produce copies of a new originator therapeutic, (2) could use disclosed clinical data to obtain independent regulatory approval of its version, and (3) could not be enjoined from doing so with the originator's patents as those patents would have been surrendered. A market exclusivity rule, by contrast, would permit full disclosure while retaining monopoly protection for the originator, since disclosed research and data could not be used to produce and register a generic version until after the expiration of the exclusivity period.

#### IV. CONCLUSION

Reform of the biologics industry to facilitate follow-on generic competition has begun with the passage of H.R. 3590, with potentially large benefits accruing to patients, insurers, and government health programs as a result. It is imperative, however, that policy-makers ensure that the new regime fosters continued innovation of new biologics products. The goal of this Article has been to persuade its audience that FDA exclusivity is superior to patent law as the primary incentive mechanism for continued biologics innovation. A comparison of these two regimes has hopefully demonstrated that FDA

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<sup>100</sup> See Eisenberg, *supra* note 17 at 380.

<sup>101</sup> *Id.* at 381-84.



exclusivity has the potential to (1) remedy the increasing anti-commons problems in upstream biomedical research, (2) alleviate costs and uncertainties associated with patenting, (3) better align incentives with clinical development of socially valuable medicines, and (4) partially counteract the tendency of firms to eschew lengthy clinical projects because of the fixed patent term. The central implication of this analysis is that continued retrenchment in the scope of available patent protections, combined with the FDA exclusivity regime contained in H.R. 3590, should be the preferred policy approach for future biologics innovation.

This Article has also explained the potential pitfalls associated with primary reliance on FDA exclusivity, and has sought to either show that those pitfalls can be overcome with simple policy prescriptions, or to question whether they are even germane to the biologics innovation context. First, incentives at the upstream stages of biomedical research are likely to remain robust because of the system of norms governing the creation and public disclosure of basic scientific inquiry and because of the potential for strategic alliances between small biotechnology companies and large drug manufacturers to incentivize the refinement of basic science into therapeutic pipelines. Second, rent dissipation is unlikely to impose major costs in the pre-clinical phases of biologics research because of the importance of multiple, independent lines of inquiry to efficient scientific progress. Rent dissipation at the clinical trials and post-marketing approval stages can be reduced or eliminated by (1) adopting a rule that the FDA cannot authorize more than one firm to conduct clinical trials on the same product, and (2) adopting a rule of FDA market exclusivity instead of data exclusivity to prevent would-be competitors from conducting rent-dissipating, redundant clinical trials to gain regulatory approval. Third, and finally, though patents play an important role in creating incentives for firms to reveal their innovations to the public, efficient disclosure of the fruits of biologics research can still be maintained in the absence of patent law if Congress adopts (1) FDA market exclusivity instead of data exclusivity, (2) a rule requiring surrender of manufacturing trade secrets and any patent rights in biologics products in exchange for FDA exclusivity, and (3) a rule requiring the FDA to disclose clinical trial data.